AMENDMENTS TO THE SPECIFICATION

Please delete the Title and replace it with the following:

~~ASSAY TO DETECT SUSTANCES USEFUL FOR THERAPY~~GTPase EFFECTORS IN ASSAYS TO DETECT PHARMACEUTICALLY USEFUL COMPOUNDS

Please delete the abstract and replace it with the following:

The present invention relates to the use of effectors/regulators for Rab and Rho GTPases in *in vitro* and *in vivo* assays~~ that recapitulate and measure the role of these effectors/regulators in membrane transport and membrane cytoskeleton interactions in the endocytic as novel~~Screening against these targets ~~to find therapeutic~~will identify drugs to prevent or inhibit cancer cell growth~~ and arrest cancer cell invasiveness~~ as well as ~~for stimulating and/or restoring~~ stimulate or restore endocytic transport and phagosome maturation in cells infected by intracellular parasites~~, which drugs are therefore useful for the therapy and optionally also the prophylaxis of cancer and infectious diseases. In addition, the present invention is also directed to kits useful as a means to detect drugs as anti-cancer and anti-infectious disease drugs~~.

Please replace the paragraph at page 2, lines 15-34, with the following:

The identification of a large number of effectors and regulators for the small GTPase Rab5 not only provides a molecular explanation for the multiplicity of functions of Rab5~~ and allow~~, but allows one to predict similar mechanisms for other Rab GTPases. Rab5 regulates a molecular network of several effector proteins, each contributing a specific function in membrane organisation, vesicle formation, vesicle and organelle movement, membrane docking and fusion. Most importantly, by functioning in a cooperative fashion Rab5 effectors modify the membrane environment and thus contribute to the biogensis of the early endosome membrane. This mode of action is exemplified by the following mechanism elucidated by the present inventors. Upon

activation by the effector/exchange factor Rabaptin Rab5/Rabex-5 complex, Rab5 locally recruits and activates phosphoinositide PI3-Kinases, leading to the generation of PI(3)P and consequently allowing the membrane recruitment o other Rab5 effectors (e.g. EEA1; see below) that bind to both Rab5:GTP and PI(3)P (Christoforidis et al., 1999b). Furthermore, Rab5 effectors are engaged in the formation of oligomeric complexes on the early endosome membrane (McBride et al., 1999). By the same criteria, other Rab proteins present in the early endosomes would be expected to recruit multiple effectors within a separate membrane environment. Consistent with this, studies using (green fluorescent protein) GFP-tagged Rab5, Rab4, and Rab11 have demonstrated that these GTPases are present in separate sub-compartments of the early endosome membrane. Endosomes are therefore organised as a mosaic of different Rab-domains created through the recruitement of specific effector proteins, which co-operatively act to generate a topologically restricted and functionally specialized environment on the endosome membrane.

Please replace the paragraph at page 26, lines 9-13, with the following:

The assay measures the activity of drugs that are capable of disrupting the association of a specific or any Rab5 effector with Rab5 in a concentration-dependent manner under the same experimental conditions that allow the interaction.~~For example, a drug x will disrupt the interaction of effector X with Rab5:GTPgS in a concentration-dependent manner. This drug will then be used as an inhibitor of effector X in the biological process X.~~